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RIGINAL ARTICLE

Assessment The Serum Progranulin Level As A Biomarker For Retinopathy In Type 2 Diabetic Patients

Yasser Samir Sheta [1]; Nermin Raafat Abdelfattahh [2]; Islam Maher Wahid [1] and Ismaeil Abdalla Habibi* [3]

[1] *Internal Medicine Department, Faculty of Medicine, Zagazig University*
[2] *Medical Biochemistry Department, Faculty of Medicine, Zagazig University*
[3] *Internal Medicine Department, Tripoli University-Libya*

***Corresponding author:**
Ismaeil Abdalla Habibi
Department of Internal Medicine, Faculty of Medicine, Tripoli University, Libya
E-mail:
belalhabibi2017@gmail.com

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ABSTRACT

Background: Micro vascular complications of T2DM are associated with severe morbidity, mortality and a huge economic burden. So, there is an important need to identify new biomarker able to identify disease onset and progression and can be used as a therapeutic target for management of these complications. The Aim of this study was to assessment the Serum progranulin level as a biomarker for the presence and severity of retinopathy in type 2 diabetic patients.

Methods: The current case-control study was carried out conducted on (48 type 2 diabetic patients) at the Internal Medicine and ophthalmology out-patient clinic of Zagazig University Hospitals, during the period from May 2019 to October 2019. All patient referred to ophthalmic out-patient clinic for fundal examination by ophthalmologist in which diabetic retinopathy was diagnosed, a complete physical examination including the measurement of height, weight, body mass index, and blood pressure (BP) was performed for all patients.

Results: The current study showed that there was a high statistically significant increase in serum PGRN level in diabetic patients with retinopathy, there was a statistically significant positive correlation between serum PGRN level with disease duration, urea, creatinine level and urinary ACR of studied retinopathy patients and also there was a high statistically significant increase in serum PGRN level in diabetic patients with proliferative retinopathy.

Conclusions: According to our results serum PGRN level could be used as a biomarker for the presence of microvascular retinal complication and to anticipate the severity of diabetic retinopathy in T2DM patients.

Keywords: Progranulin; Retinopathy; Nephropathy; Type 2 Diabetic

INTRODUCTION

Diabetes mellitus (DM) is a chronic progressive disease considering as a global epidemic. The condition is comorbid with presence of micro vascular complications [1].Diabetic retinopathy (DR) is present with development of micro albuminuria in patients with type 1 diabetes mellitus (T1DM); while, it is present only with development of macro albuminuria in patients with T2DM. Previously, micro albuminuria has been approved to be a traditional marker for diagnosis of DN, monitoring its progression, and assessment of its associated conditions as cardiovascular complications. However, recent studies have shown that albuminuria is a less accurate predictor of overt nephropathy risk than thought previously as kidney damage can progress even when micro albuminuria has regressed. Furthermore, there is a lack of a strong association between albuminuria and glomerular filtration rate (GFR). As such, there is an increasing need to find and validate an earlier and reliable biomarker to diagnose DN as an alternative to albuminuria based staging method [2].Recently activation of inflammatory processes may con-tribute to micro vascular damage with subsequent well recognized complications of diabetes. Furthermore, Lines of treatment of those complications in the future may include regulation of inflammatory processes by targeting factors that con- tribute to that vascular damage [3].Progranulin is a 68–88 kDa cysteine-rich secreted glycoprotein with varied pleiotropic actions. The secreted full length form of progranulin has anti-inflammatory action, while the proteolytically cleaved subunits by elastase called granulin peptides (GRNs) have potent pro-

inflammatory effects. It is encoded by PGRN gene and expressed by many cell types, including epithelial cells, macrophages, neurons and adipocytes [4]. Moreover, in rodents progranulin is expressed by Reno tubular epithelium but in humans the expression of PGRN in kidneys remains unknown [5]. It was originally identified as a growth factor involved in regulation of wound healing or in diseases such as cancer progression [4]. Moreover, in acute condition of ischemia–reperfusion injury, lower levels of PGRN is detected in mice kidney; and treatment with recombinant PGRN in this condition could diminish inflammation suggesting its anti-inflammatory effect. While in obesity (a chronic condition), it was recognized as an adipokine related to insulin resistance and inflammation indicating its pro-inflammatory effects and metabolic function [5]. However, until now, study for evaluating the serum PGRN as a biomarker for diabetic retinopathy and its severity among patients with T2DM seems limited and has not been investigated in details The Aim of this study was to assessment the Serum progranulin level as a biomarker for the presence and severity of retinopathy in type 2 diabetic patients.

METHODS

The current case-control study was carried out conducted on (48 type 2 diabetic patients) at the Internal Medicine and ophthalmology out-patient clinic of Zagazig University Hospitals, during the period from May 2019 to October 2019. Patients were defined according to American Diabetes Association (ADA) criteria [6] or if they were on anti-diabetic drugs. Diabetic patients were further subdivided into 24 diabetic patients with Diabetic retinopathy (DR) (control group), in addition to 24 diabetic patients without Diabetic retinopathy (control group) Diabetic retinopathy (DR) was assessed by ophthalmologist and classified based on severity into three subgroups normal, non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) using fundus examination. NPDR was diagnosed based on one or more of the following features: micro aneurysms, intra retinal hemorrhages, hard and soft exudates, venous beading and intra retinal micro vascular abnormalities while, those without these abnormalities in the retina were categorized as normal (NDR). On the other hand, PDR is considered if there was neovascularization, pre-retinal hemorrhages, vitreous hemorrhage, or pan retinal laser photo coagulation scars. The severity of DR in the worse affected eye was used for retinopathy grading. Some confusing cases were diagnosed through fundus fluorescein angiography (FFA) [7].**Inclusion criteria:** (Age 40y-70y**,** DM type 2, Duration of DM more than four years and HbA1c 7%-11%)**.**

Exclusion criteria: Those with history of malignancy, diabetic macro vascular complications, other endocrine disease which affect glucose metabolism, liver disease, other causes of renal disease, inflammatory disease, infection, urinary tract infection, pregnancy, history of drug abuse and those with T1DM were excluded from that study.

All patients were subjected to: full history taking (history for the present and past illness, medication, age, sex, and diabetes duration were obtained, family history). Physical examination [A complete physical examination including the measurement of height, weight, body mass index, and blood pressure (BP) was performed on each subject]

All patients were referred to ophthalmic out-patient clinic for fundal examination by ophthalmologist, in which diabetic retinopathy was diagnosed according to Classification of diabetic retinopathy and diabetic macular edema [8]. They were divided into two groups (after meeting inclusion criteria): Group (I): including 24 patients with diabetic retinopathy (DR). Group (II): including 24 patients with no diabetic retinopathy as a control. laboratory investigations including : [fasting blood sugar (FBS) and 2 h post prandial blood sugar (PPG), HbA1c, Kidney functions, including blood urea nitrogen (BUN) and creatinine (CREA), Urinary albumin creatinine, and serum progranulin, complete urine analysis.

PGRN: The determination of serum PGRN was carried by enzyme linked immunosorbent assays (ELISA). Five milliliter of blood samples were collected from each participant in the study after an overnight fast and then centrifuged at 3000 g for 10 min and the separated serum was stored at −80 °C until they were analyzed[9].

PGRN levels in the serum samples were determined using the Progranulin (human) ELISA Kit (Adipogen, Incheon, Korea) in duplicate with a 1:200 serum dilution according to manufacturer's protocol.

According to a previous study of Lin et al. [3] who showed that the mean of PGRN (μg/L) with normal control 45.21 ±4.75, simple diabetes mellitus 47.18 ± 4.51, early diabetic nephropathy (microalbuminuria) 53.98 ± 5.44 and clinical diabetic nephropathy,(macroalbuminuria) 86.84 ± 30.31, with p value <0.001 HS, so it we relied upon in this study, based on this assumption

Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the

World Medical Association (Declaration of Helsinki) for studies involving humans.

STATISTICAL ANALYSIS

All clinical and demographic data was recorded on investigative report form. These data analyzed using SPSS version 20. Description of quantitative variables was given as mean, and Standard deviation (SD). Chi square test (χ^2 –test) was used to compare qualitative variables between groups. The t-test was used to compare quantitative variables in parametric data. We used Kolmogorov-Smirnov and Levene tests to determine the distribution characteristics of variables and variance homogeneity. Differences between quantitative independent groups by t test or Mann Whitney. P-value (level of significance): p<0.05= significant; P<0.001= highly significant.

RESULTS

Table (1) showed that there was a high statistically significant difference among both studied diabetic cases with retinopathy and those without retinopathy regarding age (p-value<0.001), as retinopathy group were older than the other group with mean of 59.3 ± 5.9 years versus 51.2±6.1 years respectively. While both groups were matched as regard sex. Also, the duration of diabetes was statistically significant longer among cases with retinopathy than those without retinopathy with mean of 12.2 ± 4.29 versus 7.4 ± 2.45, also systolic blood pressure was significantly higher among cases with retinopathy. Also, there was 54.2% of retinopathy patients received insulin only as treatment and 33.3% received OHD, while 70.8% of patients without retinopathy medicated by OHD and only 20.8% on insulin, and the difference between both groups was statistically significant. Table (2) showed that both fasting blood sugar and glycated hemoglobin HbA1C was significantly higher among diabetic cases with retinopathy than those without retinopathy. All kidney function (urea, creatinine, ACR) measures were significantly higher among diabetic cases with retinopathy than those without retinopathy. Also, there was a high statistically significant increase in serum PGRN level among diabetic patients with retinopathy (ranged from 11.4 up to 350.9 µg/ml) than those without retinopathy, that presented with serum range of 11.4 up to 35 µg/ml only of PGRN. Table (3) showed that there was no statistically significant relation between type of retinopathy and physical examinations of the studied cases, although the duration of diabetes was longer among cases with proliferative retinopathy (PDR) but without statistically significant difference between both groups. Also, showed that fasting blood sugar or glycated hemoglobin A1C, were higher among diabetic cases with proliferative retinopathy (PDR) than in (NPDR) but it had no statistically significant value. Also, their was a high statistical significant increase in serum PGRN level among diabetic patients with proliferative retinopathy ranged from 45.3 up to 350.9 µg/ml with median of 164.5 than those with non-proliferative retinopathy, that presented with serum range of 11.4 up to 75.4 µg/ml only of PGRN.

Table 1: Baseline characteristics among the studied population

Variables	Frequency				X^2	P-value
	Cases=24 (With Retinopathy)		Controls=24 (Without Retinopathy)			
	N	%	N	%		
Sex						
Male	12	50	13	54.2	0.09	**0.773 NS**
Female	12	50	11	45.8		
	Studied groups				t-test	**P-value**
	Cases=24 (With Retinopathy)		Controls=24 (Without Retinopathy)			
Age (years) Mean ±SD Range	59.3 ± 5.9 (47-68)		51.2 ± 6.1 (40-62)		4.62	**<0.001 HS**
Duration of diabetes (years) Mean ±SD Range	12.2 ± 4.29 7-20		7.4 ± 2.45 4-12		4.75	**<0.001 HS**
Weight (Kg) Mean ±SD Range	79.6 ± 10.99 (62-110)		82.3 ± 14.1 (64-130)		0.754	**0.455 NS**

Variables	Frequency		X²	P-value
	Cases=24 (With Retinopathy)	Controls=24 (Without Retinopathy)		
Height (m)				
Mean ±SD	1.69 ± 0.1	1.68 ± 0.1	0.00	**1.0**
Range	1.59-1.78	1.54-1.86		**NS**
BMI(Kg/m²)				
Mean ±SD	28.2 ± 3.8	29.1 ± 3.8	0.842	**0.404**
Range	23.7-40.4	24.4-41.1		**NS**
SBP (mmHg)				
Mean ±SD	145.4 ± 14.4	132.7 ± 19.3	2.59	**0.01**
Range	120-170	110-160		**S**
DBP (mmHg)				
Mean ±SD	88.3 ± 8.3	83.5 ± 10.2	1.79	**0.08**
Range	70-100	70-100		**NS**
Drugs used				

Variables	Frequency				X²	P-value
	Cases=24 (With Retinopathy)		Controls=24 (Without Retinopathy)			
	N	%	N	%		
Drugs used					0.03*	**6.99**
OHD	8	33.3	17	70.8		
Insulin	13	54.2	5	20.8		
OHD + insulin	**3**	**12.5**	**2**	**8.4**		

NS: P-value>0.05 is not significant S: P-value<0.05 is significant
HS: P-value<0.001 is high significant

Table 2: laboratory data among the studied population

Variables	Studied groups		t-test	P-value
	Cases=24 (With Retinopathy)	Controls=24 (Without Retinopathy)		
FBS (mg\dl)				
Mean ±SD	205.5 ± 38.6	169.2 ± 29.8	3.65	0.001
Range	150-280	128-240		HS
Hb A1C%				
Mean ±SD	8.99 ± 1.17	7.95 ± 0.87	3.54	0.001
Range	(7.2-11)	(7-10)		HS

Variables	Studied groups		t-test\ MW*	P-value
	Cases=24 (With Retinopathy)	Controls=24 (Without Retinopathy)		
Urea (mg/dl)				
Mean ±SD	34.6 ± 8.55	24.8 ± 4.41	5.03	<0.001
Range	20-49	18-30		HS
Creatinine (mg/dl)				
Mean ±SD	0.96 ± 0.16	0.75 ± 0.19	4.7	<0.001
Range	(0.6-1.3)	(0.4-1.1)		HS
Urinary ACR (mg/gm)				
Mean ±SD	308.4 ± 575.6	21.5 ± 17.2	2.7*	0.007
Median	32.1	16.7		S
Range	6.42-2159.8	6.22-81.97		

Studied groups

Variables	Cases=24 (With Retinopathy)	Controls=24 (Without Retinopathy)	MW	P-value
PGRN (µg/ml)			**2.69**	**0.007**
Mean ±SD	**95.3 ± 108.8**	**16.2 ± 5.9**		**S**
Median	**53.5**	**12.9**		
Range	**11.4-350.9**	**11.4-35**		

S: P-value<0.05 is significant HS: P-value<0.001 is high significant

Table 3: Relation for retinopathy in the studied cases

Variables	**Studied cases (n=24)**		**t-test\ MW***	**P-value**
	PDR=10	NPDR=14		
Duration of diabetes				
Mean ±SD	14.2 ± 5.2	10.7 ± 2.9	1.71*	0.124
Range	8-20	7-16		NS
Weight (Kg)				
Mean ±SD	79.9 ± 13.8	79.4 ± 9.03	0.109	0.915
Range	62-110	70-100		NS
Height (m)				
Mean ±SD	1.7 ± 0.05	1.7 ± 0.1	0.106	0.917
Range	1.54-1.78	1.59-1.76		NS
BMI (kg/m²)				
Mean ±SD	28.3 ± 4.8	28.1 ± 3.02	0.162	0.871
Range	24.6-40.4	23.7-31.7		NS
SBP (mmHg)				
Mean ±SD	146 ± 18.4	145 ± 11.6	0.164	0.871
Range	120-170	130-160		NS
DBP (mmHg)				
Mean ±SD	91 ± 7.7	86.4 ± 8.4	1.39	0.184
Range	80-100	70-100		NS
Variables	Studied cases (n=24)		t-test	P-value
	PDR=10	NPDR=14		
FBS (mg/dl)				
Mean ±SD	214.3 ± 43.5	199.2 ± 34.98	0.905	0.377
Range	160-280	150-279		NS
Hb A1C%				
Mean ±SD	9.2 ± 1.27	8.9 ± 1.12	0.666	0.514
Range	(7.4-11)	(7.2-11)		NS
Variables	Studied cases (n=24)		MW	P-value
	PDR=10	NPDR=14		
PGRN (µg/ml)				
Mean ±SD	**188.7 ± 113.1**	**28.7 ± 23.9**	**4.69**	**0.001**
Median	**164.5**	**15.3**		**HS**
Range	**45.3-350.9**	**11.4-75.4**		

NS: P-value>0.05 is not significant

DISCUSSION

Diabetes mellitus (DM) is a chronic progressive disease considering as a global epidemic. The condition is comorbid with presence of micro vascular complications [10]. Progranulin is an evolving molecule which has both pro and anti-inflammatory properties. It plays varied functions in different tissues, cells and metabolic conditions. Firstly, it was identified as a growth factor and was considered as a potential biomarker in cancer. Also, it was considered as an adipokine associated with obesity, glucose intolerance, insulin resistance [11].Furthermore, serum PGRN level is usually low, being up regulated in the inflammatory state suggesting its involvement in chronic subclinical inflammation associated with the pathogenesis of diabetic micro angiopathy, and also, it correlated with changes in disease metrics over time which point to its potential use as a

biomarker for disease occurrence and progression in several pathologies [12].In the present study, there was a high statistically significant difference between both studied groups regarding age (p-value<0.001), which is nearly to the study of Zaky et al. [13] who found that there was a statistical significant difference among diabetic cases with retinopathy and those without retinopathy regarding age (p-value=0.032) while there was no significant difference regarding sex. But in contrast to our results the study of Lin et al., [3], who found that there was no statistical difference between the groups with regard to age their studied groups. Also, Albeltagy et al., [14] concluded that there was no significant difference between both groups as regards age.The current studies showed that there was a high statistical significant difference between studied groups regarding duration of diabetes (p value<0.001). This came in agreement with Nicoletto et al. [15] who found that the was a high statistical significant difference between their studied groups (p value <0.001). But our results were in contrast to the study of Gouliopoulos et al., [16] who concluded there was no statistical significant difference between both studied groups (diabetic cases with retinopathy and those without retinopathy) regarding duration of diabetes.

The present study, showed that there was no statistical significant difference between studied groups regarding BMI. This was in disagreement with study of Mamdouh [17] who found that there was a statistical significant difference regarding BMI index between studied groups. This difference could be contributed to the small sample size of our study. The present study, showed that a statistical significant difference between studied groups regarding the systolic blood pressure (p value = 0.01). This came in agreement with Paushter et al. [18] who found a statistical significant difference between studied groups regarding systolic blood pressure (p value <0.03). But our results were in contrast to the study of Nicoletto and Canani[15] who concluded there was no statistical significant difference between studied groups regarding systolic blood pressure.

In the present study, there was a high statistical significant difference between studied groups regarding fasting blood sugar and glycated hemoglobin A1C (p value = 0.001). This came in agreement with Jian et al. [19] who found a similar results (p value <0.001).In the current study, there was a high statistically significant difference between studied groups regarding urea and creatinine (P<0.001), while there was a statistically significant difference between studied groups regarding urinary ACR (P= 0.007).But the study of Zaky et al. [13] showed that there was a high statistically significant difference between studied groups regarding urinary ACR (p value <0.001). In the present study, there was a statistical significant difference between studied groups regarding serum PGRN level (p = 0.007). in agreement with our study, Albeltagy et al.[14] found a statistical significant difference between studied groups regarding mean serum progranulin levels in studied group (p = 032). Also the study of Ezz and Abd El A zeem [4] concluded a similar results. In contrary to our results, Mamdouh, [17], found that there was no statistical significant difference between studied groups regarding serum PGRN level (P > 0.5).In the present study, there was positive correlation between serum PGRN level with FBS and HbA1c but not significant. While Lin et al. [3] reported that there was no remarkable correlation was found between PGRN and FBS, HbA1c. On the other hand, this came in disagreement with Li et al. [21] and Qu et al. [22] whom found that there was a significant positive correlation between PGRN and parameter of glucose metabolism namely Hb A1C, fasting plasma glucose in DM patients. In the present study, there was statistically significant positive correlation between serum PGRN level with duration of diabetes. This came in agreement with Colhoun and Marcovecchio [22] who reported significant positive correlation of PGRN with duration of DM. Albeltagy et al. [14] and Lin et al. [3] both found that there was a highly significant positive correlation between serum PGRN and disease duration,. In the current study, there was highly significant positive correlation between serum PGRN level with kidney function tests(s.Cr, urea and ACR) (p value = 0.003) between studied groups. This agree with Shafaei et al. [12] who found there was positive correlation between progranulin and other renal parameters (sCr, urea and ACR). Also, this was in consistency with Lin et al. [3] study that showed that there was a significant positive correlation between serum PGRN and sCr.. In the current study, there was a statistical significant difference between studied groups regarding urea. Which in agreement with the study of Lin et al. [3] who found that there was a statistical significant difference between both groups regarding urea. In the present study, there was no statistical significant difference between studied groups regarding creatinine. Which in disagreement with the study of Shafaei et al. [12] who found that there was a statistical significant difference between both groups regarding creatinine.

CONCLUSIONS

According to our results serum PGRN level could be used as a biomarker for the presence of microvascular retinal complication and to

anticipate the severity of diabetic retinopathy in T2DM patients.

RECOMMENDATIONS

Further studies are needed to understand the exact mechanisms underlying the increase of progranulin in patients with diabetic micro angiopathy and further studies using larger populations and longer duration will be needed to confirm our observations and to validate the current findings.

Conflict of Interest: None.

Financial disclosure: None.

REFERENCES

1- Huang L, Xie Y, Dai S, Zheng H. Neutrophil-to-lymphocyte ratio in diabetic microangiopathy. Int J Clin Exp Pathol 2017; 10 (2):1223–1232.

2. Karlberg C, Falk C, Green A, Sjølie AK, Grauslund J. Proliferative retinopathy predicts nephropathy: a 25-year follow-up study of type 1 diabetic patients. Acta Diabetol. 2012; 49:263–8.

3- Lin X, Zhou B, Huixia L, Jiali L, Junhui D, Weijin Z, et al. Serum levels of progranulin are closely associated with microvascular complication in type 2 diabetes. Dis Markers. 2015; 357279.

4. Ezz MK, Abd El Azeem EM. Assessment of progranulin in Egyptian type 2 diabetic patients as a novel biomarker for diabetic nephropathy. Int J Biosci. 2016; 9 (6):350–9.

5. Zhou M, Tang W, Fu Y, Xu X, Wang Z, Lu Y, et al. Progranulin protects against renal ischemia/reperfu-Sion injury in mice. Kidney Int. 2015; 87:918–29.

6- American Diabetes Association. Diagnosis and classification of diaberes mellitus. Diabetes Care. 2014;37 (1): S81–90.

7- Mowatt L. (2013). Diabetic retinopathy and its risk factors at the University Hospital in Jamaica. Middle East Afr J Ophthalmol 2013, 20 (4), 321.-326

8- Wu L, Fernandez-Loaiza P, Sauma J, Hernandez-Bogantes E, Masis M. Classification of diabetic retinopathy and diabetic macular edema. World J Diabetes 2013, 4 (6): 290-294.

9- Thurner L, Preuss KD, Fadle N, Regitz E, Klemm P, Zaks M et al. Progranulin antibodies in autoimmune diseases. J Autoimmun. 2013; 42: 29-38.

10- Huang L, Huang L, Xie Y, Dai S, Zheng H. Neutrophil-to-lymphocyte ratio in diabetic microangiopathy. Int J Clin Exp Pathol 2017; 10(2):1223–1232.

11- Ezz MK, Abd El Azeem EM. Assessment of progranulin in Egyptian type 2 diabetic patients as a novel biomarker for diabetic nephropathy. Int J Biosci 2016; 9 (6):350–9.

12-Shafaei A, Marjani A, and Khoshnia M. Serum Progranulin Levels in Type 2 Diabetic Patients with Metabolic Syndrome. Rom J Intern Med 2016; 54(4): 211-216.

13- Zaky DS, Kareema YA, Abd-Rabo SA, Nagwa AG, Mayada FS. Serum Level of Progranulin and Microvascular Complication in Type 2 Diabetes. Inter J Diabet Res 2018; 7 (3): 57-62.

14- Albeltagy ES, Hammour AE, Albeltagy SA. Potential value of serum Progranulin as a biomarker for the presence and severity of micro vascular complications among Egyptian patients with type 2 diabetes mellitus. J Diabet Metabolic Dis 2019; 18 (1): 217.

15- Nicoletto BB, Canani LH. The role of progranulin in diabetes and kidney disease. Diabetol Metab Syndr 2015; 7(1): 117.

16- Gouliopoulos NS, Kalogeropoulos C, Lavaris A, Rouvas A, Asproudis I, Garmpi A et al. Association of serum inflammatory markers and diabetic retinopathy: a review of literature. Eur Rev Med Pharmacol Sci 2018; 22 (21): 7113-7128.

17- Mamdouh MA. The Relation between Microvascular Complications of Type II Diabetes with Levels of Serum Progranulin. Egypt J Med Res 2020, 1(1): 29-42.

18- Paushter D, Du H, Feng T, Hu F. The lysosomal function of progranulin, a guardian against neurodegeneration. Acta Neuropathol 2018; 136 (1): 1-17.

19- Jian J, Li G, Hettinghouse A, Liu C. Progranulin: A key player in autoimmune diseases. Cytokine. 2018; 101: 48-55.

20- Korolczuk A. Progranulin a new adipokine at the crossroads of metabolic syndrome, diabetes, dyslipidemia and hypertension. Curr Pharm Des 2017, 23 (10), 1533-1539.

21- Li H, Zhou B, Xu L, Liu J, Zang W, Wu S et al. Circulating PGRN is significantly associated with systemic insulin sensitivity and autophagic activity in metabolic syndrome. Endocrinology 2014; 155: 3493–3507.

22- Qu H, Deng H, Hu Z. Plasma progranulin concentrations are increased in patients with type 2 diabetes and obesity and correlated with insulin resistance. Mediators Inflamm. 2013; 360190

23- Colhoun HM, Marcovecchio ML. Biomarkers of diabetic kidney disease. Diabetologia 2018; 61 (5): 996-1011.

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